

DNA bubble dynamics as a quantum Coulomb problem

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We study the dynamics of denaturation bubbles in double-stranded DNA on the basis of the Poland-Scheraga model. We demonstrate that the associated Fokker-Planck equation is equivalent to a Coulomb problem. Below the melting temperature the bubble lifetime is associated with the continuum of scattering states of the repulsive Coulomb potential, at the melting temperature the Coulomb potential vanishes and the underlying first exit dynamics exhibits a long time power law tail, above the melting temperature, corresponding to an attractive Coulomb potential, the long time dynamics is controlled by the lowest bound state. Correlations and finite size effects are discussed.

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Introduction. The dynamics of bubble formation in double-stranded DNA (dsDNA) is a problem of high current interest in biological and statistical physics. Under physiological conditions the Watson-Crick double helix is the equilibrium structure, its stability effected by hydrogen-bonding of base-pairs and stacking between nearest neighbor pairs of base-pairs [1, 2]. By variation of temperature or pH-value double-stranded DNA progressively denatures, yielding regions of single-stranded DNA (ssDNA), until the double-strand is fully denatured. This is the helix-coil transition associated with the melting temperature T_m [3].

Subject to thermal fluctuations dsDNA spontaneously unzips and forms flexible single-stranded DNA bubbles ranging in size from a few to some hundred broken base-pairs, depending on T and salt conditions [3, 4, 5]. Assuming that the bubble-forming dynamics takes place on a slower time scale than the equilibration of the ssDNA strands constituting the bubbles, this DNA-breathing can be interpreted as a random walk in the 1D coordinate x , the number of denatured base-pairs.

On the basis of the Poland-Scheraga model for DNA-melting [10] DNA-breathing has been studied in terms of a continuous Fokker-Planck equation [6, 7], and of a discrete master equation and stochastic simulation [8, 9]. In the present Letter we show that the Fokker-Planck equation for bubble breathing is equivalent to a quantum Coulomb problem with a repulsive potential above T_m and an attractive potential below T_m . This mapping allows us to discuss DNA bubble dynamics in terms of the spectrum of a 'hydrogen-like' system and to derive several exact results such as the exact scaling of the bubble survival behavior and the associated correlations.

Static and dynamic model. The Poland-Scheraga free energy for the bubble statistics has the form [3, 5, 7]

$$\mathcal{F} = \gamma_0 + \gamma x + c \ln x, \quad (1)$$

where $x \geq 0$ is the bubble size in units of base pairs.

We here assume a continuum formulation and imply a cutoff for $x \sim 1$. γ_0 is the free energy barrier for initial bubble formation, γx is the free energy for the dissociation of x base pairs, and $c \ln x$ the entropy loss factor associated with the formation of a closed polymer ring. The free energy density $\gamma = \gamma_1(1 - T/T_m)$, where T_m is the melting temperature. From experimental data one extracts approximate values for the parameters. In units of kT_r with reference temperature $T_r = 37^\circ\text{C}$, we have $\gamma_0 \approx 10kT_r$, $\gamma_1 \approx 4kT_r$, and $c \approx 2kT_r$; the melting temperature for standard salt conditions is in the range $T_m \approx 70 - 100^\circ\text{C}$, depending on the relative content of weaker AT and stronger GC Watson-Crick base-pairs.

The stochastic bubble dynamics is governed by the Langevin equation with Gaussian white noise $\xi(t)$,

$$\frac{dx}{dt} = -D \frac{d\mathcal{F}}{dx} + \xi, \quad \langle \xi \xi \rangle(t) = 2DkT\delta(t), \quad (2)$$

where the kinetic coefficient D of dimension $(kT_r)^{-1}\text{s}^{-1}$ sets the overall time scale of the dynamics: $[DkT_r]^{-1} \sim \mu\text{s}$. With dimensionless parameters $\mu = c/2kT$ and $\epsilon = (\gamma_1/2kT)(T/T_m - 1)$, and measuring time in units of μs , the Fokker-Planck equation corresponding to (2) reads

$$\frac{\partial P}{\partial t} = \frac{\partial}{\partial x} \left(\frac{\mu}{x} - \epsilon \right) P + \frac{1}{2} \frac{\partial^2 P}{\partial x^2}. \quad (3)$$

Note that close to the physiological temperature T_r , $\mu \approx 1$ and $\epsilon \approx 2(T/T_m - 1)$.

General results. Eliminating the first order term by means of the substitution $P = e^{\epsilon x} x^{-\mu} \tilde{P}$, \tilde{P} satisfies

$$-\frac{\partial \tilde{P}}{\partial t} = -\frac{1}{2} \frac{\partial^2 \tilde{P}}{\partial x^2} + \left(\frac{\mu(\mu+1)}{2x^2} - \frac{\mu\epsilon}{x} + \frac{\epsilon^2}{2} \right) \tilde{P}. \quad (4)$$

This is the imaginary time Schrödinger equation for a particle with unit mass in the potential $V(x) = \mu(\mu+1)/2x^2 - \mu\epsilon/x + \epsilon^2/2$, i.e., subject to the centrifugal barrier $\mu(\mu+1)/x^2$ for an orbital state with angular momentum μ and Coulomb potential $-\mu\epsilon/x$. Introducing the

Hamiltonian $H = -(1/2)d^2/dx^2 + V(x)$ and expanding \hat{P} on the normalized eigenstates Ψ_n , $H\Psi_n = E_n\Psi_n$, the transition probability $P(x, x_0, t)$ from initial bubble size x_0 to a final bubble size x at time t yields in closed form,

$$P(x, x_0, t) = e^{\epsilon(x-x_0)} \left(\frac{x}{x_0}\right)^{-\mu} \sum_n e^{-E_n t} \Psi_n(x) \Psi_n(x_0). \quad (5)$$

Here the completeness of Ψ_n ensures the initial condition $P(x, x_0, 0) = \delta(x-x_0)$. Moreover, in order to account for the absorbing boundary condition for vanishing bubble size we choose $\Psi_n(0) = 0$. We also note that for a finite strand of length L , i.e., a maximum bubble size of L , we have in addition the absorbing condition $\Psi_n(L) = 0$ for complete denaturation. Expression (5) is the basis for our discussion of DNA-breathing, relating the dynamics to the spectrum of eigenstates, i.e., the bound and scattering states of the corresponding Coulomb problem [11].

The transition probability P is controlled by the Coulomb spectrum. Below the melting temperature T_m ($\epsilon \propto (T/T_m - 1) < 0$), the Coulomb problem is repulsive and the states form a continuum, corresponding to a random walk in bubble size terminating in bubble closure ($x = 0$). At the melting temperature ($\epsilon = 0$), the Coulomb potential is absent and the continuum of states is governed by the centrifugal barrier alone, including the limiting case of a regular random walk. Above the melting temperature ($\epsilon > 0$), the Coulomb potential is attractive and can trap an infinity of bound states; at long times the lowest bound state dominates the bubble dynamics, corresponding to denaturation of the DNA chain. In Fig. 1 we depict the potential in the two cases $\epsilon \gtrless 0$.

(i) *Long times for $T \leq T_m$.* At long times and fixed x and x_0 , it follows from (5) that the transition probability is controlled by the bottom of the energy spectrum. Below and at T_m the spectrum is continuous with lower bound $\epsilon^2/2$. Setting $E_k = \epsilon^2/2 + k^2/2$ in terms of the wave number k and noting that $\Psi_k(x) \propto (kx)^{1+\mu}$ for small kx we have $P \propto \exp(-|\epsilon|(x-x_0))(x/x_0)^{-\mu} \exp(-\epsilon^2 t/2) \int_0^\infty dk \exp(-k^2 t/2) (k^2 x x_0)^{1+\mu}$, and consequently by a simple scaling argument the long-time expression for the probability distribution

$$P(x, x_0, t) \simeq x x_0^{1+2\mu} e^{-|\epsilon|(x-x_0)} e^{-\epsilon^2 t/2} t^{-3/2-\mu}. \quad (6)$$

The lifetime of a bubble of initial size x_0 created at $t = 0$ follows from Eq. (6) by calculating the first passage time density (FPTD) as time derivative of the survival probability, $W(t) = -\int_0^\infty dx \partial P / \partial t$ [12], or, via Eq. (3), $W(t) = (1/2)[\partial P / \partial x + (2\mu/x - 2\epsilon)P]_{x=0}$. This produces

$$W(t) \simeq x_0^{1+2\mu} e^{|\epsilon|x_0} e^{-\epsilon^2 t/2} t^{-3/2-\mu}. \quad (7)$$

Below T_m , $\epsilon < 0$ and the FPTD $W(t)$ decays exponentially. The characteristic time scale is set by

$$\tau = 2/\epsilon^2 \propto (T_m - T)^{-2}, \quad (8)$$

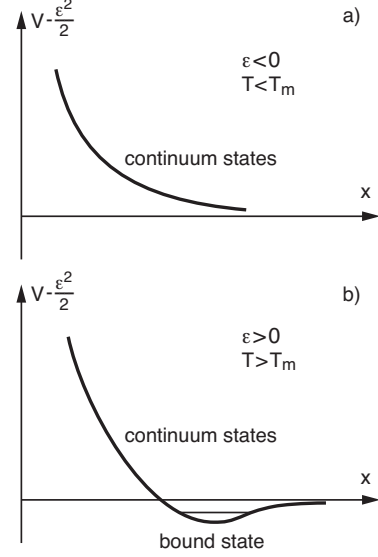


FIG. 1: Schematic of the potential $V(x) - \epsilon^2/2$ of the Schrödinger Eq. (4). a) $T < T_m$: The potential is repulsive, yielding a continuous spectrum. The bubble fluctuations correspond to a Brownian walk process in bubble size x before collapse at $x = 0$. b) $T > T_m$. The potential is attractive and can trap a series of bound states. At long times the lowest bound state indicated in the figure controls the behavior. The bubbles increase in size leading to denaturation.

that diverges as one approaches T_m . Finally, from Eq. (6) we infer that $P(x, t) \propto \exp(-c_1|\epsilon|(x + c_2|\epsilon|t))$ with constants $c_i > 0$, indicating that the profile of the distribution has a drift $\sim |\epsilon|$ towards bubble closure at $x = 0$.

At T_m ($\epsilon = 0$) the FPTD falls off like a power law, $W(t) \propto t^{-\alpha}$ with scaling exponent

$$\alpha = 3/2 + \mu. \quad (9)$$

The parameter $\mu = c/2kT$ (with $\mu \approx 1$ at $T \approx T_r$) is associated with the entropy loss of a closed polymer loop. Ignoring the logarithmic entropic effects ($\mu = 0$) we obtain $\alpha = 3/2$, characteristic of an unbiased random walk [7]. From (7) we also conclude that the mean bubble lifetime scales like

$$\tau_{\text{mean}} \propto x_0/|\epsilon| \propto x_0(T_m - T)^{-1}, \quad (10)$$

that diverges as the temperature is raised towards T_m .

(ii) *Long times for $T > T_m$.* Above T_m ($\epsilon > 0$) the transition probability P is controlled by the lowest bound states in the attractive Coulomb potential. For the discrete spectrum we have $E_n = \epsilon^2/2(1 - (\mu/(\mu + n))^2)$, $n = 1, 2, \dots$. The lowest state is thus given by $E_1 = \epsilon^2(\mu + 1/2)/(\mu + 1)^2$, and the corresponding nodeless normalized bound state by $\Psi_1(x) = Ax^{1+\mu} \exp(-\mu\epsilon x/(\mu + 1))$ with normalization constant $A^2 = [2\mu\epsilon/(\mu + 1)]^{2\mu+3}/\Gamma(2\mu + 3)$ [11]. This bound

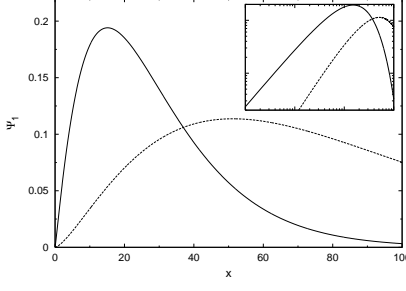


FIG. 2: Lowest bound state of the attractive well in $V(x)$ for $T = 10T_r$ (full line) and $T = 2.2T_r$ (dashed); with $T_m = 2T_r$. Inset: log-log plot showing the power-law increase at $x = 0$.

state is localized at $\sim 1/(T - T_m)$ and thus recedes to infinity as we approach the melting temperature. In Fig. 2 we depict the lowest bound state Ψ_1 . From (5) we have $P(x, x_0, t) \sim e^{\epsilon(x-x_0)}(x/x_0)^{-\mu}e^{-E_1 t}\Psi_1(x)\Psi_1(x_0)$, and we note that the dominant contribution to the distribution originates from the region where the bound state peaks, i.e., at $\sim 1/(T - T_m)$. Inserting in (5) we obtain

$$P(x, x_0, t) = A^2 x_0^{1+2\mu} e^{(\epsilon/(1+\mu))(x-x_0(1+2\mu))} \times e^{-\epsilon^2(1+2\mu)t/2(1+\mu)^2}, \quad (11)$$

after some reduction. Note from (11) that the profile of the distribution drifts towards larger bubble sizes with velocity $\sim \epsilon$. The associated FPTD becomes

$$W(t) = A^2(1/2 + \mu)x_0^{1+2\mu}e^{-\epsilon x_0(1+2\mu)/(1+\mu)} \times e^{-\epsilon^2 t(1+2\mu)/2(1+\mu)^2}.$$

Exact result at T_m . At the melting temperature ($\epsilon = 0$) the bubble dynamics problem is equivalent to the case of a noisy finite-time singularity studied in Ref. [13]. The eigenstates of H are Bessel functions, $\Psi_k(x) = (kx)^{1/2}J_{1/2+\mu}(kx)$, and we obtain after inserting in (5) the distribution

$$P(x, x_0, t) = \frac{x^{1/2-\mu}}{x_0^{1/2-\mu}} \int_0^\infty dk e^{-k^2 t/2} k^2 J_{1/2+\mu}(kx) \times J_{1/2+\mu}(kx_0), \quad (12)$$

or, by a well-known identity [14], the explicit expression

$$P(x, x_0, t) = \left(\frac{x}{x_0}\right)^{-\mu} (xx_0)^{1/2} t^{-1} e^{-(x^2+x_0^2)/2t} \times I_{1/2+\mu}(xx_0/t), \quad (13)$$

where I_ν is the Bessel function of imaginary argument [14]. From (13) we infer the FPTD

$$W(t) = \frac{2x_0^{1+2\mu}}{\Gamma(1/2 + \mu)} e^{-x_0^2/2t} (2t)^{-3/2-\mu}, \quad (14)$$

whose maximum at $t = x_0^2/(3 + 2\mu)$ assumes the value

$$W_{\max} = \frac{2}{\Gamma(1/2 + \mu)} \left(\frac{2e}{3 + 2\mu}\right)^{-3/2-\mu} x_0^{-1/2}. \quad (15)$$

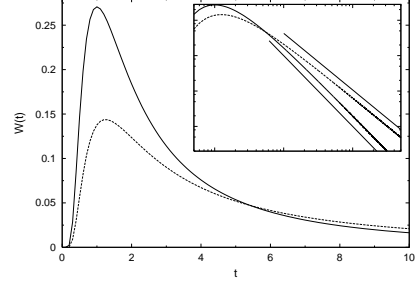


FIG. 3: Bubble lifetime distribution $W(t)$ from Eq. (14) for $T_m = 2T_r$ (full line) and $T_m = 10T_r$ (dashed). Inset: log-log plot of the power-law behavior at long t , with slopes -2 and -1.6 , as indicated by the straight lines.

In Fig. 3 we show the zero-size bubble distribution for two different melting temperatures corresponding to different power-law tails of the FPTD $W(t)$.

Correlations and finite size effects. In typical experiments measuring the fluorescence correlation of a tagged base-pair, DNA bubble dynamics can be measured on the single molecule level [15]. The correlation function $C(t)$ is proportional to the integrated survival probability $C(t) \propto \int_0^L P(x, x_0, t) dx$, where L is the chain length [16]. From the definition of the FPTD we see that indeed $C(t) = 1 - \int_0^t W(t) dt$. We find three cases:

(i) Below T_m ($\epsilon < 0$) we obtain from Eq. (6) $C(t) = 1 - x_0^{1+2\mu} e^{|\epsilon|x_0} \int_0^t e^{-\epsilon^2 t'/2} (t')^{-3/2-\mu} dt'$, or, in terms of the incomplete Gamma function γ [14],

$$C(t) = 1 - x_0^{1+2\mu} e^{|\epsilon|x_0} (\epsilon^2/2)^{1/2+\mu} \gamma(-1/2 - \mu, \epsilon^2 t/2). \quad (16)$$

With $\gamma(\alpha, x) = \Gamma(\alpha) - x^{\alpha-1}e^{-x}$ for $x \rightarrow \infty$ we obtain

$$C(t) = \text{const.} + x_0^{1+2\mu} \epsilon^{-2} e^{|\epsilon|x_0} t^{-3/2-\mu} e^{-\epsilon^2 t/2} \quad (17)$$

for large t . Note that the basic time scale of the correlations is set by $\epsilon^{-2} \propto (T_m - T)^{-2}$. For $t \ll \epsilon^{-2}$ the correlations show a power law behavior, $C(t) \propto t^{-3/2-\mu}$; at long times $t \gg \epsilon^{-2}$ the correlations fall off exponentially. The size of the time window showing power law behavior increases as T_m is approached. In frequency space the structure function $\tilde{C}(\omega) = \int \exp(i\omega t) C(t) dt$ has a Lorentzian line shape for $|\omega| \ll \epsilon^2$, and power law tails for $|\omega| \gg \epsilon^2$:

$$\tilde{C}(\omega) \sim \begin{cases} x_0^{1+2\mu} e^{|\epsilon|x_0} (\omega^2 + (\epsilon^2/2)^2)^{-1}, & \text{for } |\omega| \ll \epsilon^2, \\ x_0^{1+2\mu} e^{|\epsilon|x_0} |\epsilon|^{-2} |\omega|^{1/2+\mu}, & \text{for } |\omega| \gg \epsilon^2. \end{cases} \quad (18)$$

(ii) At T_m ($\epsilon = 0$) the exact expression for the FPTD (14) combined with relation $C(t) = -\int_t^\infty W dt$ yield

$$C(t) = 1 - \frac{\Gamma(1/2 + \mu, x_0^2/2t)}{\Gamma(1/2 + \mu)}. \quad (19)$$

For short times $t \rightarrow 0$ the behavior

$$C(t) = 1 - \frac{(x_0^2/2)^{\mu-1/2}}{\Gamma(1/2+\mu)} t^{1/2-\mu} e^{-x_0^2/2t} \quad (20)$$

obtains, while in the long time limit $t \rightarrow \infty$,

$$C(t) = \frac{2(x_0^2)^{1/2+\mu}}{(1+2\mu)\Gamma(1/2+\mu)} t^{-1/2-\mu}. \quad (21)$$

(iii) Above T_m ($\epsilon > 0$) the DNA chain eventually fully denatures, and the correlations diverge in the thermodynamic limit. We can, however, at long times estimate the size dependence for a chain of length L . From the general expression (5) we find

$$C(t) \simeq e^{-\epsilon x_0} x_0^\mu \sum_n e^{-E_n t} \Psi_n(x_0) \int_0^L e^{\epsilon x} x^{-\mu} \Psi_n(x) dx \quad (22)$$

With the lowest bound state $\Psi_1(x) = A x^{1+\mu} \exp(-\mu \epsilon x / (\mu + 1))$ of energy $E_1 = \epsilon^2(\mu + 1/2)/(\mu + 1)^2$, and after integration over x , we obtain

$$C(t) \propto A^2 e^{-\epsilon x_0(2\mu+1)/(\mu+1)} e^{-\epsilon^2((\mu+1/2)/(\mu+1)^2)t} x_0^{1+2\mu} \times (1+\mu) \epsilon^{-2} \left[1 + (L\epsilon/(1+\mu) - 1) e^{\epsilon L/(1+\mu)} \right]. \quad (23)$$

The correlations decay exponentially with the time constant $\sim \epsilon^{-2}(\mu + 1)^2/(2\mu + 1)$. In frequency space the structure function has a Lorentzian lineshape of width $\sim \epsilon^2(2\mu + 1)/(\mu + 1)^2$, and for the size dependence one obtains

$$C(t) \sim \begin{cases} L e^{\epsilon L/(1+\mu)}, & \text{for } \epsilon L/(1+\mu) \gg 1, \\ L \epsilon/(1+\mu), & \text{for } \epsilon L/(1+\mu) \ll 1 \end{cases} \quad (24)$$

Note that close to T_m the correlation function $C(t) \propto L$.

Summary and conclusion. We demonstrated that the breathing dynamics of thermally induced denaturation bubbles forming spontaneously in double-stranded DNA can be mapped onto the imaginary time Schrödinger equation of the quantum Coulomb problem. This mapping allows to calculate the distribution of bubble lifetimes and the associated correlation functions, below, at, and above the melting temperature of the DNA helix-coil transition. Moreover, at the melting transition, the DNA bubble-breathing was revealed to correspond to a one-dimensional finite time singularity.

Our analysis reveals non-trivial scaling of the first passage time density quantifying the survival of a bubble after its original nucleation. The associated critical exponents depend on the parameter μ stemming from the entropy loss factor of the flexible bubble, and therefore on the ratio T_r/T of reference and actual temperature. This correction through μ decreases with increasing T . FPTD

and correlations also depend on the difference $T/T_m - 1$, and therefore explicitly on the melting temperature T_m (and thus the relative content of AT or GC base-pairs). We also obtained the critical dependence of the characteristic time scales of bubble survival and correlations on the difference $T - T_m$. The finite size-dependence of the correlation function was recovered, as well.

The mapping of the of DNA-breathing onto the quantum Coulomb problem provides a new way to investigate its physical properties, in particular, in the range above the melting transition, $T > T_m$. The detailed study of the DNA bubble breathing problem is of particular interest as the bubble dynamics provides a test case for new approaches in small scale statistical mechanical systems where the fluctuations of DNA bubbles are accessible on the single molecule level in real time.

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